Amendment to the Claims

This listing of claims will replace all prior versions, and listings, of claims in the application:

1. (Currently Amended) A method of making a substituted pyrazolopyrimidine, or pharmaceutically acceptable salt thereof, the method comprising reacting an aminopyrazole compound or a salt thereof with a substituted 1-oxo-2-propenyl-compound or a salt thereof under acidic conditions in a reaction medium including a two-phase mixture of an aqueous solution and a water-immiscible organic liquid.

2. (Original) The method of claim 1 wherein the reaction mixture further includes at least one phase-transfer agent.

3. (Currently amended) The method of claim ~~2~~ 1 wherein the ~~at least one phase-transfer agent~~ aqueous phase includes a water-soluble salt.

4. (Original) The method of claim 3 wherein the water soluble salt includes a salt selected from the group consisting of sodium chloride, sodium bromide, sodium sulfate, sodium hydrogen phosphate, sodium dihydrogen phosphate, sodium phosphate, sodium acetate, ammonium acetate, sodium tartrate, sodium benzoate, sodium phthalate and mixtures thereof.

5. (Original) The method of claim 1 wherein the acidic conditions are prepared by the addition of at least one acid including an acid selected from the group consisting of at least one mineral acid, at least one organic acid and mixtures, thereof.

6. (Original) The method of claim 5 wherein the at least one acid includes at least one acid selected from the group consisting of hydrochloric, hydrobromic, hydrofluoric, sulfuric, acetic, formic, methanesulfonic, p-toluenesulfonic, trifluoroacetic, hexanesulfonic, heptafluorobutyric, perchloric, nitric, phosphoric acid and mixtures thereof.

7. (Original) The method of claim 1 wherein the aqueous phase includes water.

8. (Original) The method of claim 1 wherein the aqueous phase includes at least one water miscible solvent or polymer selected from the group consisting of formamide, acetamide, 1-methyl-2-pyrrolidinone, DMF, DMAC, DMSO, hexamethylphosphoramide, hexamethylphosphortriamide, methylsulfone, sulfolane, 1-methylpropandiol, methanol, ethanol, propanol, butanol, acetonitrile, propionitrile, THF, glycol ethers, acetone, dioxane, nitromethane, nitroethane, polyethylene glycol, polyoxyethylene, polyglycerol, polyvinylpyrrolidone, polyvinyl alcohol and mixtures thereof.

9. (Original) The method of claim 1 wherein the water immiscible organic liquid includes an organic liquid selected from the group consisting of chloroform, dichloromethane, hexane and hexane

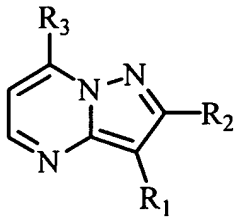
compounds, heptane, cyclohexane, methylcyclohexane, anisole, fluorobenzene, chlorobenzene, toluene, xylene and xylene compounds, diethylether, tert-butylmethylether, n-propyl formate, ethyl acetate, butyl acetate, propyl acetate, isoamyl acetate, 2-butanone, 2-hexanone, 3-methyl-2-pentanone, 4-methyl-2-pentanone, pinacolone, 2-heptanone, acetophenone, cyclohexanone, cyclopentanone, long-chained alcohols, for example; decanol, dodecanol and mixtures thereof.

10. (Original) The method of claim 1 further including extracting the pyrazolopyrimidine from the water immiscible organic liquid.

11. (Original) The method of claim 10 further included recrystallizing the extracted pyrazolopyrimidine.

12. -14. (Canceled) The method of claim 1 wherein the pyrazolopyrimidine is zaleplon.

15. (Currently amended) ~~A~~ The method of Claim 1, wherein the ~~making a~~ substituted pyrazolopyrimidine~~, or pharmaceutically acceptable salt thereof,~~ comprises a compound of Formula I,



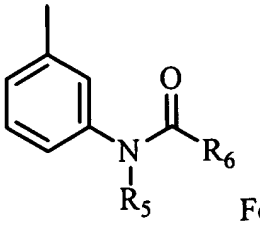
Formula I

wherein R_1 is selected from the group consisting of hydrogen, fluoro, chloro, bromo, formyl, carboxyl, cyano, hydroxymethyl, N-hydroxyformimidoyl and R_4CO- wherein R_4 is selected from the group consisting of hydrogen; alkyl(C_1-C_6); alkoxy(C_1-C_6); unsubstituted phenyl; phenyl mono- or disubstituted by halogen, alkyl(C_1 –C_3) or alkoxy(C_1 –C_3); phenyl (C_1 – C_3), phenyl substituted by trifluoromethyl, alkylthio(C_1 –C_3), alkylamino(C_1 –C_3), dialkylamino(C_1 –C_3), methylenedioxy, alkylsulfonyl(C_1 –C_3) or alkanoylamino(C_1 –C_3); naphthalenyl; thiazolyl; biphenyl; thienyl; furanyl; pyridinyl; substituted thiazolyl; substituted biphenyl; substituted thienyl; and substituted pyridinyl, wherein the substituents are selected from one or two of the groups consisting of halogen, alkyl(C_1 –C_3) and alkoxy(C_1 –C_3);

R_2 is selected from the group consisting of hydrogen, fluoro, chloro, bromo, cyano, cyanomethyl, carbamoyl or alkyl (C_1 –C_3); and

wherein R_3 is selected from the group consisting of phenyl; o-trifluoromethylphenyl; m-trifluoromethylphenyl; m-methoxyphenyl; pyridyl; pyridyl N-oxide; thienyl; furanyl; and

substituted phenyl, wherein one or more of the positions is substituted by a group represented by Formula II



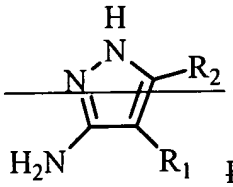
Formula II

wherein R_5 is selected from the group consisting of hydrogen, alkyl(C_1-C_6), alkenyl(C_2-C_6), alkynyl, cycloalkyl(C_3-C_6)methyl, -CH_2OCH_3, –$CH_2CH_2OCH_3$,–CH_2CH_2OH, –$CH_2CHOHCH_2OH$, and –$[CH_2CH_2O]_{n=10\text{-}120}$; and

R_6 is selected from the group consisting of alkyl(C_1-C_6), cycloalkyl(C_3-C_6), -O-alkyl(C_1-C_6), -NH-alkyl(C_1-C_3), -N-dialkyl(C_1-C_3), -(CH_2)nO-alkyl(C_1-C_3), -$(CH_2)_n$NH-alkyl(C_1-C_3) and -$(CH_2)_n$N-dialkyl(C_1-C_3), where n is an integer 1 to 3 inclusive~~;~~

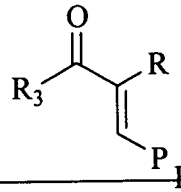
~~the method comprising:~~

~~reacting a compound of Formula III or a salt thereof with a compound of Formula IV or a salt thereof under acidic conditions in a reaction medium including a two-phase mixture of an aqueous solution and a water-immiscible organic liquid, wherein Formula III is~~



~~Formula III~~

~~and Formula IV is~~



~~Formula IV~~

~~P is selected from the group consisting of -Oac, -OR, -SR and -NR'R; and~~

~~R and R' are selected from the group consisting of hydrogen, alkyl(C_1-C_6) and cyclic alkyl~~.

16. (Canceled)

17. (Currently amended) The method of claim 2 ~~16~~ wherein the at least one phase transfer agent is selected from the group consisting of ~~includes but are not limited to the following~~: Aliquat® 336, ALKANOL®s, Polyethylene(PEG) esters and diesters, polypropylene glycol (PPG) and PEG-PPG copolymers, tetraalkylammonium salts, tetraalkylphosphonium salts, N-alkylpyridinium salts, sodium stearate, sodium palmitate, sodium laurate.

18.-27. (Canceled)

28. (Currently amended) The method of claim 15 wherein Formula I is selected from the group consisting of:

N-[3-(3-cyanopyrazolo[1,5-a]pyrimidin-7-yl)phenyl]-N-ethylpropanamide;

N-[3-(3-cyanopyrazolo[1,5-a]pyrimidin-7-yl)phenyl]-N-ethylacetamide;

N-[3-(3-cyanopyrazolo[1,5-a]pyrimidin-7-yl)phenyl]-N-propylacetamide;

N-[3-(3-cyanopyrazolo[1,5-a]pyrimidin-7-yl)phenyl]-N-(polyethyleneglycol)acetamide;

N-[3-(3-cyanopyrazolo[1,5-a]pyrimidin-7-yl)phenyl]-N-(methoxyethyl)acetamide;

N-[3-(3-cyanopyrazolo[1,5-a]pyrimidin-7-yl)phenyl]-N-(hydroxyethyl)acetamide;

N-[3-(3-cyanopyrazolo[1,5-a]pyrimidin-7-yl)phenyl]-N-(1',2'-propanediol)acetamide;

N-[3-(3-cyanopyrazolo[1,5-a]pyrimidin-7-yl)phenyl]-N-(1'-propanol)acetamide;

N-[3-(3-cyanopyrazolo[1,5-a]pyrimidin-7-yl)phenyl]-N-(2'-propanol)acetamide;

[3-(3-cyanopyrazolo[1,5-a]pyrimidin-7-yl)phenyl]methylcarbamic acid, methyl ester;

7-[3-[(methoxycarbonyl)methylamino]phenyl]pyrazolo[1,5-a]pyrimidine-3-carboxylic acid, ethyl ester;

[3-(3-cyanopyrazolo[1,5-a]pyrimidin-7-yl)phenyl]ethylcarbamic acid, methyl ester;

ethyl(3-pyrazolo[1,5-a]pyrimidin-7-ylphenyl)carbamic acid, ethyl ester;

[3-(3-chloropyrazolo[1,5-a]pyrimidin-7-yl)phenyl]ethylcarbamic acid, ethyl ester;

N-[3-(3-cyanopyrazolo[1,5-a]pyrimidin-7-yl)phenyl]-N-2-propenylacetamide;

N-[3-(3-cyanopyrazolo[1,5-a]pyrimidin-7-yl)phenyl]-N-2-propynylacetamide;

N-[3-(3-cyanopyrazolo[1,5-a]pyrimidin-7-yl)phenyl]-N-methylacetamide;

7-(3-pyridyl)pyrazolo[1,5-a]pyrimidine;

7-(3-pyridyl)pyrazolo[1,5-a]pyrimidine-3-carbonitrile;

2-ethyl-7-(3-pyridyl)pyrazolo[1,5-a]pyrimidine-3-carbonitrile;

7-(3-pyridyl)pyrazolo[1,5-a]pyrimidine-3-carboxylic acid ethyl ester;

2-ethyl-7-(3-pyridyl)pyrazolo[1,5-a]pyrimidine-3-carboxylic acid ethyl ester;

7-(3-thienyl)pyrazolo[1,5-a]pyrimidine-3-carboxylic acid ethyl ester;

7-(3-thienyl)pyrazolo[1,5-a]pyrimidine-3-carbonitrile;

6-methyl-7-(3-pyridyl)pyrazolo[1,5-a]pyrimidine-3-carbonitrile;

3-bromo-7-(3-pyridyl)pyrazolo[1,5-a]pyrimidine;

3-chloro-7-(3-pyridyl)pyrazolo[1,5-a]pyrimidine;

7-(3-pyridyl)pyrazolo[1,5-a]pyrimidine, pyridine-1-oxide;

2-methyl-7-(3-pyridyl)pyrazolo[1,5-a]pyrimidine-3-carbonitrile;

2,6-dimethyl-7-(3-pyridyl)pyrazolo[1,5-a]pyrimidine-3-carbonitrile;

2-methyl-7-(3-pyridyl)pyrazolo[1,5-a]pyrimidine-3-carboxylic acid ethyl ester;

N-[3-(3-benzoylpyrazolo[1,5-a]pyrimidin-7-yl)phenyl]-N-methylcyclobutanecarboxamide;

N-[3-(3-benzoylpyrazolo[1,5-a]pyrimidin-7-yl)phenyl]-N-methylcyclopropanecarboxamide;

[3-(3-benzoylpyrazolo[1,5-a]pyrimidin-7-yl)phenyl]methylcarbamic acid, methyl ester;

N-methyl-N-[3-[3-(2-thienylcarbonyl)pyrazolo[1,5-a]pyrimidin-7-yl]phenyl]-cyclopropanecarboxamide;

[3-(3-benzoylpyrazolo[1,5-a]pyrimidin-7-yl)phenyl]methylcarbamic acid, methyl ester;

[3-(3-benzoylpyrazolo[1,5-a]pyrimidin-7-yl)phenyl]ethylcarbamic acid, ethyl ester;

N-2-propenyl-N-[3-[3-(2-thienylcarbonyl)pyrazolo[1,5-a]pyrimidin-7-yl]phenyl]acetamide;

ethyl[3-[3-(2-thienylcarbonyl)pyrazolo[1,5-a]pyrimidin-7-yl]phenyl]carbamic acid, ethyl ester;

N-[3-(3-benzoylpyrazolo[1,5-a]pyrimidin-7-yl)phenyl]-N-2-propenylacetamide;

N-[3-(3-benzoylpyrazolo[1,5-a]pyrimidin-7-yl)phenyl]-N-2-propynylacetamide;

N-methyl-N-(3-{3-[2-thienylcarbonyl]pyrazolo[1, 5-a]-pyrimidin-7-yl}phenyl)acetamide;

7-(α,α,α–trifluoro-m-tolyl)pyrazolo[1,5-a]pyrimidine-3-carbonitrile;

ethyl 7 (α,α,α–trifluoro-m-tolyl)pyrazolo[1,5-a]pyrimidine-3-carboxylate;

methyl 7-(α,α,α–trifluoro-m-tolyl)pyrazolo[1,5-a]pyrimidin-3-yl ketone;

7-(α,α,α–trifluoro-m-tolyl)pyrazolo[1,5-a]pyrimidine-3-carboxaldehyde oxime;

7-(m-methoxyphenyl)pyrazolo[1,5-a]pyrimidine-3-carbonitrile;

3-(methoxymethyl)-7-(α,α,α–trifluoro-m-tolyl)pyrazolo-[1 ,5-a]pyrimidine;

3-bromo-7-(α,α,α–trifluoro-m-tolyl)pyrazolo[1,5-a]pyrimidine;

2-cyano-7(α,α,α–trifluoro-m-tolyl)pyrazolo[1,5-a]pyrimidine-3-carbonitrile;

3-cyano-7-(α,α,α–trifluoro-m-tolyl)pyrazolo[1,5-a]-pyrimidine-2-acetonitrile;

3-methyl-7-(α,α,α–trifluoro-m-tolyl)pyrazolo[1,5-a]pyrimidine;

ethyl 7-(m-tolyl)pyrazolo[1,5-a]pyrimidine-3-carboxylate;

ethyl 7-(3,4-xylyl)pyrazolo[1,5-a]pyrimidine-3-carboxylate;

ethyl 7-(p-ethylphenyl)pyrazolo[1,5-a]pyrimidine-3-carboxylate;

ethyl 7-(3,4-dimethoxyphenyl)pyrazolo[1,5-a]pyrimidine-3-carboxylate;

7-(m-Fluorophenyl)pyrazolo[1,5-a]pyrimidine-3-carbonitrile;

5-Phenylpyrazolo[1,5-a]pyrimidine; and

5-(α,α,α–Trifluoro-m-tolyl)pyrazolo[1,5-a]pyrimidine.

29. (Original) A method for making zaleplon, the method comprising:

reacting N-[3-[3-(dimethylamino)-1-oxo-2-propenyl]phenyl]-N-ethylacetamide with 3-amino-4-cyanopyrazole under acidic conditions in a reaction medium including a two-phase mixture of an aqueous solution and a water-immiscible organic liquid.

30. (Currently amended) The method of claim 29 wherein the reaction mixture further includes at least one phase transfer agent selected from the group consisting of: Aliquat® 336, ALKANOL®s, Polyethylene(PEG) esters and diesters, polypropylene glycol (PPG) and PEG-PPG copolymers, tetraalkylammonium salts, tetraalkylphosphonium salts, N-alkylpyridinium salts, sodium stearate, sodium palmitate, sodium laurate.

31. (Canceled)

32. (Currently amended) The method of claim ~~31~~ 29 wherein the aqueous phase includes a water soluble salt ~~includes a salt~~ selected from the group consisting of sodium chloride, sodium bromide, sodium sulfate, sodium hydrogen phosphate, sodium dihydrogen phosphate, sodium phosphate, sodium acetate, ammonium acetate, sodium tartrate, sodium benzoate, sodium phthalate and mixtures thereof.

33. (Original) The method of claim 29 wherein the acidic conditions are prepared by the addition of at least one acid including an acid selected from the group consisting of at least one mineral acid, at least one organic acid and mixtures thereof.

34. (Original) The method of claim 33 wherein the at least one acid includes at least one acid selected from the group consisting of hydrochloric, hydrobromic, hydrofluoric, sulfuric, acetic, formic, methanesulfonic, p-toluenesulfonic, trifluoroacetic, hexanesulfonic, heptafluorobutyric, perchloric, nitric, phosphoric acid and mixtures thereof.

35. (Original) The method of claim 29 wherein the aqueous phase includes water.

36. (Original) The method of claim 29 wherein the aqueous phase includes at least one water miscible solvent or polymer selected from the group consisting of formamide, acetamide, 1-methyl-2-pyrrolidinone, DMF, DMAC, DMSO, hexamethylphosphoramide, hexamethylphosphortriamide, methylsulfone, sulfolane, 1-methylpropandiol, methanol, ethanol, propanol, butanol, acetonitrile, propionitrile, THF, glycol ethers, acetone, dioxane, nitromethane, nitroethane, polyethylene glycol, polyoxyethylene, polyglycerol, polyvinylpyrrolidone, polyvinyl alcohol and mixtures thereof.

37. (Original) The method of claim 29 wherein the water immiscible organic liquid includes an organic liquid selected from the group consisting of chloroform, dichloromethane, hexane and hexane compounds, heptane, cyclohexane, methylcyclohexane, anisole, fluorobenzene, chlorobenzene, toluene, xylene and xylene compounds, diethylether, tert-butylmethylether, n-propyl formate, ethyl acetate, butyl acetate, propyl acetate, isoamyl acetate, 2-butanone, 2-hexanone, 3-methyl-2-pentanone, 4-methyl-2-pentanone, pinacolone, 2-heptanone, acetophenone, cyclohexanone, cyclopentanone, long-chained alcohols, for example; decanol, dodecanol and mixtures thereof.

38. (Original) The method of claim 29 further including extracting the zaleplon from the water immiscible organic liquid.

39. (Original) The method of claim 38 further included recrystallizing the extracted zaleplon.

40. (Original) A method for making Indiplon™, the method comprising:

reacting N-[3-[3-(dimethylamino)-1-oxo-2-propenyl]phenyl]-N-methylacetamide with (3-amino-1H-pyrazol-4-yl)-2-thienylmethanone under acidic conditions in a reaction medium including a two-phase mixture of an aqueous solution and a water-immiscible organic liquid.

41. (Currently amended) The method of claim 40 wherein the reaction mixture further includes at least one phase transfer agent selected from the group consisting of: Aliquat® 336, ALKANOL®s, Polyethylene(PEG) esters and diesters, polypropylene glycol (PPG) and PEG-

PPG copolymers, tetraalkylammonium salts, tetraalkylphosphonium salts, N-alkylpyridinium salts, sodium stearate, sodium palmitate, sodium laurate.

42. (Canceled)

43. (Currently amended) The method of claim ~~42~~ 40 wherein the aqueous phase includes a water soluble salt ~~includes a salt~~ selected from the group consisting of sodium chloride, sodium bromide, sodium sulfate, sodium hydrogen phosphate, sodium dihydrogen phosphate, sodium phosphate, sodium acetate, ammonium acetate, sodium tartrate, sodium benzoate, sodium phthalate and mixtures thereof.

44. (Original) The method of claim 40 wherein the acidic conditions are prepared by the addition of at least one acid including an acid selected from the group consisting of at least one mineral acid, at least one organic acid and mixtures thereof.

45. (Original) The method of claim 44 wherein the at least one acid includes at least one acid selected from the group consisting of hydrochloric, hydrobromic, hydrofluoric, sulfuric, acetic, formic, methanesulfonic, p-toluenesulfonic, trifluoroacetic, hexanesulfonic, heptafluorobutyric, perchloric, nitric, phosphoric acid and mixtures thereof.

46. (Original) The method of claim 40 wherein the aqueous phase includes water.

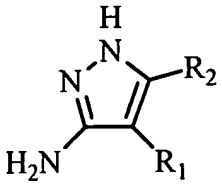
47. (Original) The method of claim 40 wherein the aqueous phase includes at least one water miscible solvent selected from the group consisting of formamide, acetamide, 1-methyl-2-pyrrolidinone, DMF, DMAC, DMSO, hexamethylphosphoramide, hexamethylphosphortriamide, methylsulfone, sulfolane, 1-methylpropandiol, methanol, ethanol, propanol, butanol, acetonitrile, propionitrile, THF, glycol ethers, acetone, dioxane, nitromethane, nitroethane, polyethylene glycol, polyoxyethylene, polyglycerol, polyvinylpyrrolidone, polyvinyl alcohol and mixtures thereof..

48. (Original) The method of claim 40 wherein the water immiscible organic liquid includes an organic liquid selected from the group consisting of chloroform, dichloromethane, hexane and hexane compounds, heptane, cyclohexane, methylcyclohexane, anisole, fluorobenzene, chlorobenzene, toluene, xylene and xylene compounds, diethylether, tert-butylmethylether, n-propyl formate, ethyl acetate, butyl acetate, propyl acetate, isoamyl acetate, 2-butanone, 2-hexanone, 3-methyl-2-pentanone, 4-methyl-2-pentanone, pinacolone, 2-heptanone, acetophenone, cyclohexanone, cyclopentanone, long-chained alcohols, for example; decanol, dodecanol and mixtures thereof.

49. (Original) The method of claim 40 further including extracting Indiplon™ from the water immiscible organic liquid.

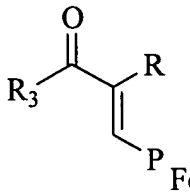
50. (Original) The method of claim 40 further included recrystallizing the extracted Indiplon™.

51. (New) The method of Claim 15, wherein the aminopyrazole compound comprises a compound of Formula III:



Formula III

52. (New) The method of Claim 15, wherein the substituted 1-oxo-2-propenyl-compound comprises a compound of Formula IV:



Formula IV

wherein P is selected from the group consisting of –Oac, -OR, -SR and –NR'R; and

R and R' are selected from the group consisting of hydrogen, alkyl(C_1-C_6) and cyclic alkyl.